Cancer stem cells and microenvironment in prostate cancer progression.

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Public Summary:
The results suggested that the cancer associated fibroblasts in the prostate tumor microenvironment can contribute to the biologic properties of the CSCs and by this account may play a major role in prostate tumorigenesis and progression. Thus, it would be important now to identify the paracrine and/or juxtacrine factors that are responsible for the stimulation of the cancer stem cells.

Scientific Abstract:
For a study of interactions between the cancer-associated fibroblasts (CAFs) and the putative prostate cancer stem cells (CSCs), we used a conditional Pten deletion mouse model of prostatic adenocarcinoma to isolate both CAF cultures and CSC-enriched cell fractions from the primary tumors. The CSC subpopulation exhibited a collective phenotype of Lin(-)/SCA-1(hi)/CD49f(hi)/p63 (hi)/CK5 (hi)/AR (lo)/CK18 (lo)/Survivin (hi)/Runx2 (hi) and contained cells with the ability to both self-renew and differentiate into basal and luminal cells in vitro. The spheroids generated from the CSC-enriched subpopulation mimicked the glandular structures that could be produced from a similarly isolated cell fraction from the normal mouse prostate. The efficiency of spheroid formation was found to be influenced differentially by the nature of the fibroblasts that were co-cultured in the 3-D system. The growth and differentiation properties of the CSCs were significantly more enhanced by factors released from CAFs relative to normal prostate fibroblasts (NPFs). Additionally, increased commitment to differentiation to the luminal cell lineage was noted when CAFs were present. When CSCs admixed with either CAFs or NPFs were examined for formation of prostatic glandular structures in renal grafts in vivo, the lesions formed were generally more in numbers in the presence of CAFs than NPFs. Furthermore, lesions formed with CAFs often displayed tumor-like complex histopathology and contained increased numbers of proliferating cells. Taken together, the results suggested that the CAFs in the prostate tumor microenvironment can contribute to the biologic properties of the CSCs and by this account may play a major role in prostate tumorigenesis and progression. Thus, it would be important now to identify the paracrine and/or juxtacrine factors that are responsible for the stimulation of the cancer stem cells.